



POSTER PRESENTATION

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Variants of PBEF predispose to systemic sclerosis and pulmonary arterial hypertension development

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Aim

Pre B-cell colony-enhancing factor (PBEF) is intricately involved in inflammation and fibrosis, functional polymorphisms of PBEF have been previously shown to influence PBEF expression and pulmonary damage. Systemic sclerosis (SSc) is a disease in which inflammation, fibrosis and pulmonary deterioration are prominent hallmarks. Therefore we here investigate the role of the *PBEF* -1001T>G and *PBEF* -1543C>T polymorphisms in the genetic predisposition to systemic sclerosis (SSc) susceptibility and pulmonary involvement.

Patients and methods

We genotyped DNA from 2737 SSc patients and 1913 matched healthy controls, both from 8 different ethnic populations. Genotyping was performed using custom Taqman 5' allelic discrimination assays. In addition, PBEF serum expression levels were measured by ELISA and correlated with genotypes.

Results

In two separate populations and in a meta-analysis, the combined *PBEF* -1543CC -1001TT genotype, hence carrying no minor alleles, was found associated with SSc susceptibility ($P=0.009$ OR 1.20 (95% CI 1.05-

1.37). In addition, these subjects showed an increased decline in forced vital capacity (FVC) over 15 years follow-up ($P=0.02$) (HR 1.64, 95%CI: 1.02-2.64) and a higher PBEF serum concentration ($P<0.01$), compared to carriers of minor alleles. On the other hand, patients with genotype *PBEF* -1001TT were at lower risk for PAH development within 15 years of disease onset compared to the carriers with genotypes *PBEF* -1001GG and *PBEF* -1001TG ($P<0.001$) (HR 3.29, 95% CI: 1.52-7.12).

Conclusions

Our data identify PBEF as a novel candidate gene that influences SSc susceptibility, pulmonary function and the development of PAH.

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